In the Claims:

Please cancel claims 58-61 and 64-158 without prejudice.

Please add new claims 159-164.

Please amend claim 63 as follows:

1. **(Original)** A humanized immunoglobulin light chain comprising (i) variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and (ii) a variable framework region from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(a) a residue that non-covalently binds antigen directly;

(b) a residue adjacent to a CDR;

(c) a CDR-interacting residue; and

(d) a residue participating in the VL-VH interface.

2. **(Original)** A humanized immunoglobulin heavy chain comprising (i) variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and (ii) a variable framework region from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(a) a residue that non-covalently binds antigen directly;

(b) a residue adjacent to a CDR;

(c) a CDR-interacting residue; and

(d) a residue participating in the VL-VH interface.

3. **(Original)** The light chain of claim 1, wherein a CDR-interacting residue is identified by modeling the 3D6 light chain based on the solved structure of 1CR9.

4. **(Original)** The light chain of claim 1, wherein a CDR-interacting residue is identified by modeling the 3D6 light chain based on the solved structure of 1NLD.

5. **(Original)** The heavy chain of claim 2, wherein a CDR-interacting residue is identified by modeling the 3D6 heavy chain based on the solved structure of 1OPG.

6. **(Original)** A humanized immunoglobulin light chain comprising (i) variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and (ii) a variable framework region from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is a residue capable of affecting light chain variable region conformation or function as identified by analysis of a three-dimensional model of the 3D6 immunoglobulin light chain variable region.

7. **(Original)** A humanized immunoglobulin heavy chain comprising (i) variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and (ii) variable framework region from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is a residue capable of affecting heavy chain variable region conformation or function as identified by analysis of a three-dimensional model of the 3D6 immunoglobulin heavy chain variable region.

8. **(Original)** The light chain of claim 6, wherein the framework residue is selected from the group consisting of a residue capable of interacting with antigen, a residue proximal to the antigen binding site, a residue capable of interacting with a CDR, a residue adjacent to a CDR, a residue within 6 Å of a CDR residue, a canonical residue, a vernier zone residue, an interchain packing residue, a rare residue, and a glycoslyation site residue on the surface of the structural model.

9. **(Original)** The heavy chain of claim 7, wherein the framework residue is selected from the group consisting of a residue capable of interacting with antigen, a residue proximal to the antigen binding site, a residue capable of interacting with a CDR, a residue adjacent to a CDR, a residue within 6 Å of a CDR residue, a canonical residue, a vernier zone residue, an interchain packing residue, an unusual residue, and a glycoslyation site residue on the surface of the structural model.

10. **(Original)** The light chain of claim 6 or 8, wherein the framework residue is identified by modeling the 3D6 light chain based on the solved structure of 1CR9.

11. **(Original)** The light chain of claim 6 or 8, wherein the frame work residue is identified by modeling the 3D6 light chain based on the solved structure of 1NLD.

12. **(Original)** The heavy chain of claim 7 or 9, wherein the framework residue is identified by modeling the 3D6 heavy chain based on the solved structure of 1OPG.

13. **(Original)** A humanized immunoglobulin light chain comprising (i) variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and (ii) a variable framework region from a human acceptor immunoglobulin light chain, provided that at least one framework residue selected from the group consisting of L1, L2, L36 and L46 (Kabat numbering convention) is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence.

14. **(Original)** A humanized immunoglobulin heavy chain comprising (i) variable region complementarity determining regions from the 3D6 heavy chain variable region sequence set forth as SEQ ID NO:4, and (ii) a variable framework regions from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue selected from the group consisting of H49, H93 and H94 (Kabat numbering convention) is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence.

15. **(Previously presented)** The light chain of any one claims 1, 6, and 13, wherein the human acceptor light chain is of the subtype kappa II (Kabat convention).

16. **(Previously presented)** The heavy chain of any one claims 2, 7, and 14, wherein the human acceptor heavy chain is of the subtype III (Kabat convention).

17. **(Original)** The light chain of claim 15, wherein the human acceptor light chain is selected from the group consisting of Kabat ID 019230, Kabat ID 005131, Kabat ID 005058, Kabat ID 005057, Kabat ID 005059, Kabat ID U21040 and Kabat ID U41645.

18. **(Original)** The light chain of claim 15, wherein the human acceptor light chain is Kabat ID 019230.

19. **(Original)** The heavy chain of claim 16, wherein the human acceptor heavy chain is selected from the group consisting of Kabat ID 045919, Kabat ID 000459, Kabat ID 000553, Kabat ID 000386 and Kabat ID M23691.

20. **(Original)** The heavy chain of claim 16, wherein the human acceptor heavy chain is Kabat ID 045919.

21. **(Previously presented)** The light chain of any one of claims 1, 6, and 13, wherein at least one rare human framework residue is substituted with an amino acid residue which is common for human variable light chain sequences at that position.

22. **(Previously presented)** The light chain of claim 1, 6, and 13, wherein at least one rare human framework residue is substituted with a corresponding amino acid residue from a germline variable light chain sequence.

23. **(Original)** The light chain of claim 22, wherein the germline variable light chain sequence is selected from the group consisting of A1, A17, A18, A2, and A19.

24. **(Previously presented)** The heavy chain of any one of claims 2, 7, and 14, wherein at least one rare human framework residue is substituted with an amino acid residue which is common for human variable heavy chain sequences at that position.

25. **(Previously presented)** The heavy chain of any one of claims 2, 7, and 14, wherein at least one rare human framework residue is substituted with a corresponding amino acid residue from a germline variable heavy chain sequence.

26. **(Original)** The heavy chain of claim 25, wherein the germline variable heavy chain sequence is selected from the group consisting of VH3-48, VH3-23, VH3-7, VH3-21 and VH3-11.

27. **(Original)** The heavy chain of claim 25, wherein the germline variable heavy chain sequence is VH3-23.

28. **(Previously presented)** The light chain of claim 21, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human light chain variable region sequences in the light chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the light chain variable region subgroup.

29. **(Previously presented)** The heavy chain of claim 24, wherein the rare framework residue is selected based on occurrence at that position in less than 10% of human heavy chain variable region sequences in the heavy chain variable region subgroup, and the common residue is selected based on an occurrence at that position in greater than 50% of sequences in the heavy chain variable region subgroup.

30. **(Original)** A light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L1, L2, L36 and L46 (Kabat numbering convention) from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin.

31. **(Original)** A heavy chain comprising the complementarity determining regions (CDRs) and variable framework residues H49, H93 and H94 (Kabat numbering convention) from the monoclonal antibody 3D6 heavy chain, wherein the remainder of the heavy chain is from a human immunoglobulin.

32. **(Previously presented)** A humanized immunoglobulin comprising a light chain selected from the group consisting of:

(a) a light chain comprising variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and comprising variable framework regions from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is selected from the group consisting of
(i) a residue that non-covalently binds antigen directly;
(ii) a residue adjacent to a CDR;
(iii) a CDR-interacting residue; and
(iv) a residue participating in the VL-VH interface;

(b) a light chain comprising variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and comprising variable framework regions from a human acceptor immunoglobulin light chain sequence, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence, wherein the framework residue is a residue capable of affecting light chain variable region conformation or function as identified by analysis of a three-dimensional model of the variable region;

(c) a light chain comprising variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin light chain variable region sequence set forth as SEQ ID NO:2, and a variable framework regions from a human acceptor immunoglobulin light chain, provided that at least one framework residue selected from the group consisting of L1, L2, L36 and L46 (Kabat

numbering convention) is substituted with the corresponding amino acid residue from the mouse 3D6 light chain variable region sequence; and

(d) a light chain comprising the complementarity determining regions (CDRs) and variable region framework residues L1, L2, L36 and L46 (Kabat numbering convention) from the monoclonal antibody 3D6 light chain, wherein the remainder of the light chain is from a human immunoglobulin;

and a heavy chain selected from the group consisting of:

(a) heavy chain comprising variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and comprising variable framework regions from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is selected from the group consisting of:

(i) a residue that non-covalently binds antigen directly;

(ii) a residue adjacent to a CDR;

(iii) a CDR-interacting residue; and

(iv) a residue participating in the VL-VH interface;

(b) a heavy chain comprising variable region complementarity determining regions (CDRs) from the 3D6 immunoglobulin heavy chain variable region sequence set forth as SEQ ID NO:4, and comprising variable framework regions from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence, wherein the framework residue is a residue capable of affecting heavy chain variable region conformation or function as identified by analysis of a three-dimensional model of the variable region;

(c) a heavy chain comprising variable region complementarity determining regions from the 3D6 heavy chain variable region sequence set forth as SEQ ID NO:4, and a variable framework regions from a human acceptor immunoglobulin heavy chain, provided that at least one framework residue selected from the group consisting of H49, H93 and H94 (Kabat numbering

convention) is substituted with the corresponding amino acid residue from the mouse 3D6 heavy chain variable region sequence; and

(d) a heavy chain comprising the complementarity determining regions (CDRs) and variable framework residues H49, H93 and H94 (Kabat numbering convention) from the monoclonal antibody 3D6 heavy chain, wherein the remainder of the heavy chain is from a human immunoglobulin;

or an antigen binding fragment of said immunoglobulin.

33. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}.

34. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^8 M^{-1}.

35. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^9 M^{-1}.

36. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, wherein the heavy chain isotype is γ1.

37. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which binds to both soluble beta amyloid peptide (Aβ) and aggregated Aβ.

38. **(Original)** The immunoglobulin of claim 37, wherein the soluble beta amyloid peptide (Aβ) is disaggregated Aβ.

39. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which mediates phagocytosis of beta amyloid peptide (Aβ).

40. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which crosses the blood-brain barrier in a subject.

41. **(Original)** The immunoglobulin or antigen binding fragment of claim 32, which reduces both beta amyloid peptide (Aβ) burden and neuritic dystrophy in a subject.

42. **(Original)** A humanized immunoglobulin comprising a humanized heavy chain and a humanized light chain, wherein

(a) the humanized light chain comprises three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of the mouse 3D6 immunoglobulin light chain variable domain designated SEQ ID NO:2, and a variable region framework from a human light chain variable region framework sequence provided that at least one position selected from a first group consisting of L1, L2, L36 and L46 (Kabat numbering convention) is occupied by the same amino acid residue present in the equivalent position of the mouse 3D6 immunoglobulin light chain variable region framework; and

(b) the humanized heavy chain comprises three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of the mouse 3D6 immunoglobulin heavy chain variable domain designated SEQ ID NO:4, and a variable region framework from a human heavy chain variable region framework sequence provided that at least one position selected from a second group consisting of H49, H93 and H94 (Kabat numbering convention) is occupied by the same amino acid residue present in the equivalent position of the mouse 3D6 immunoglobulin heavy chain variable region framework;

wherein the humanized immunoglobulin specifically binds to beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}, wherein the 3D6 immunoglobulin has the

light chain with a variable domain designated SEQ ID NO:2 and the heavy chain with a variable domain designated SEQ ID NO: 4.

43. **(Original)** The humanized immunoglobulin of claim 42, wherein human light chain variable region framework is from a kappa light chain variable region.

44. **(Original)** The humanized immunoglobulin of claim 42, wherein human heavy chain variable region framework is from an IgG1 heavy chain variable region.

45. **(Original)** The humanized immunoglobulin of claim 42, wherein the humanized light chain variable region framework is from a light chain selected from the group consisting of Kabat ID 019230, Kabat ID 005131, Kabat ID 005058, Kabat ID 005057, Kabat ID 005059, Kabat ID U21040 and Kabat ID U41645.

46. **(Original)** The humanized immunoglobulin of claim 42, wherein the humanized heavy chain variable region framework is from a heavy chain selected from the group consisting of Kabat ID 045919, Kabat ID 000459, Kabat ID 000553, Kabat ID 000386 and Kabat ID M23691.

47. **(Original)** The humanized immunoglobulin of claim 42, wherein the humanized light chain variable region framework is identical to the Kabat ID 019230 light chain variable region framework sequence except for the positions from the first group, and the heavy chain variable region framework is identical to the Kabat ID 045919 heavy chain variable region framework sequence except for the positions from the second group.

48. **(Original)** The humanized immunoglobulin of claim 42, wherein the humanized light chain comprises complementarity determining regions that are identical to the corresponding complementarity determining regions of the mouse 3D6 heavy chain, and the humanized heavy chain comprises complementarity determining regions that are identical to the corresponding complementarity determining regions of the mouse 3D6 heavy chain.

49. **(Previously presented)** A humanized immunoglobulin comprising the complementarity determining regions (CDR1, CDR2 and CDR3) of the 3D6 variable light chain sequence set forth as SEQ ID NO:2.

50. **(Previously presented)** A humanized immunoglobulin comprising the complementarity determining regions (CDR1, CDR2 and CDR3) of the 3D6 variable heavy chain sequence set forth as SEQ ID NO:4.

51. **(Previously presented)** A humanized immunoglobulin, or antigen-binding fragment thereof, which specifically binds to beta amyloid peptide (Aβ), comprising a variable region comprising complementarity determining regions (CDRs) corresponding to CDRs from the mouse 3D6 immunoglobulin.

52. **(Previously presented)** A humanized immunoglobulin which binds beta amyloid peptide (Aβ) with an affinity of at least 10^7 M^{-1} comprising:

(a) a light chain variable domain comprising murine 3D6 complementarity determining region (CDR) amino acid residues and human VL subgroup II variable domain framework region (FR) amino acid residues; and

(b) a heavy chain variable domain comprising murine 3D6 complementarity determining region (CDR) amino acid residues and human VH subgroup III variable domain framework region (FR) amino acid residues.

53. **(Currently amended)** A chimeric immunoglobulin comprising murine 3D6 variable ~~region complementarity determining regions (CDRs) from the 3D6 immunoglobulin variable region sequences set forth as SEQ ID NO:2 or SEQ ID NO:4, and variable framework~~ regions and constant regions from a human acceptor immunoglobulin.

54. **(Original)** An immunoglobulin, or antigen-binding fragment thereof, comprising a variable heavy chain region as set forth in SEQ ID NO:8 and a variable light chain region as set forth in SEQ ID NO:5.

55. **(Original)** An immunoglobulin, or antigen-binding fragment thereof, comprising a variable heavy chain region as set forth in SEQ ID NO:12 and a light chain region as set forth in SEQ ID NO:11.

56. **(Original)** An immunoglobulin comprising a variable heavy chain region as set forth in SEQ ID NO:8, a variable light chain region as set forth in SEQ ID NO:5, and constant regions from IgG1.

57. **(Original)** An immunoglobulin comprising a variable heavy chain region as set forth in SEQ ID NO:12, a light chain region as set forth in SEQ ID NO:11, and constant regions from IgG1.

Claims 58-61. **(Cancelled)**

62. **(Previously presented)** A pharmaceutical composition comprising the immunoglobulin of any one of claims 32, 42, and 49-52 and a pharmaceutical carrier.

63. **(Currently amended)** An isolated polypeptide ~~selected from the group consisting of:~~

(a) ~~a polypeptide~~ comprising a fragment of SEQ ID NO:2 selected from the group consisting of amino acids 24-39 of SEQ ID NO:2, amino acids 55-61 of SEQ ID NO:2 and amino acids 94-102 of SEQ ID NO:2;

~~(b) a polypeptide comprising amino acids 24-39 of SEQ ID NO:2, amino acids 55-61 of SEQ ID NO:2 and amino acids 94-102 of SEQ ID NO:2;~~

~~(c) a polypeptide comprising a fragment of SEQ ID NO:4 selected from the group consisting of amino acids 31-35 of SEQ ID NO:4, amino acids 50-66 of SEQ ID NO:4 and amino acids 99-107 of SEQ ID NO:4;~~

~~(d) a polypeptide comprising amino acids 31-35 of SEQ ID NO:4, amino acids 50-66 of SEQ ID NO:4 and amino acids 99-107 of SEQ ID NO:4;~~

~~(e) a polypeptide comprising the amino acid sequence of SEQ ID NO:2;~~

~~(f) a polypeptide comprising the amino acid sequence of SEQ ID NO:4; and~~

~~(g) a polypeptide comprising residues 1-112 of the amino acid sequence of SEQ ID NO:2 or comprising residues 1-119 of the amino acid sequence of SEQ ID NO:4.~~

Claims 64-68. **(Cancelled)**

69. **(Original)** A variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, said variant comprising at least one conservative amino acid substitution, wherein the variant retains the ability to direct specific binding to beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}.

70. **(Original)** A variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:4, said variant comprising at least one conservative amino acid substitution, wherein the variant retains the ability to specifically bind beta amyloid peptide (Aβ) with a binding affinity of at least 10^7 M^{-1}.

Claims 71-158. **(Cancelled)**

159. **(New)** An isolated polypeptide comprising amino acids 24-39 of SEQ ID NO:2, amino acids 55-61 of SEQ ID NO:2 and amino acids 94-102 of SEQ ID NO:2.

160. **(New)** An isolated polypeptide comprising a fragment of SEQ ID NO:4 selected from the group consisting of amino acids 31-35 of SEQ ID NO:4, amino acids 50-66 of SEQ ID NO:4 and amino acids 99-107 of SEQ ID NO:4.

161. **(New)** An isolated polypeptide comprising amino acids 31-35 of SEQ ID NO:4, amino acids 50-66 of SEQ ID NO:4 and amino acids 99-107 of SEQ ID NO:4.

162. **(New)** An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2.

163. **(New)** An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:4.

164. **(New)** An isolated polypeptide comprising residues 1-112 of the amino acid sequence of SEQ ID NO:2 or comprising residues 1-119 of the amino acid sequence of SEQ ID NO:4.